



Attorney Docket No.: YOR920000435US1  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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**Patent Application**

Applicant(s) Floratos et al.  
Docket No.: YOR920000435US1  
Serial No.: 09/712,638  
Filing Date: November 14, 2000  
Group: 1631  
Examiner: C. Dune Ly

I hereby certify that this paper is being deposited on this date with the U.S. Postal Service as first class mail addressed to the Commissioner for Patents, P.O. Box 1450, VA 22313-1450

Signature: *Susan Futina* Date: July 12, 2005

Title: Unsupervised Building and Exploitation of Composite Descriptors

TRANSMITTAL OF REPLY BRIEF

Mail Stop Appeal Brief - Patents  
Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith are the following documents relating to the above-identified patent application:

(1) Reply Brief

In the event of non-payment or improper payment of a required fee, the Commissioner is authorized to charge or to credit **IBM Corporation Deposit Account No. 50-0510** as required to correct the error. A duplicate copy of this letter is enclosed.

Respectfully submitted,

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Dated: July 12, 2005

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Patent Application**

Applicant(s) Rigoutsos et al.  
Docket No.: YOR920000435US1  
Serial No.: 09/712,638  
Filing Date: November 14, 2000  
Group: 1631  
Examiner: C.D. Ly

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Signature: Susan Futane Date: July 12, 2005

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REPLY BRIEF

Mail Stop Appeal Brief – Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Appellants hereby reply to the Examiner's Answer, mailed May 12, 2005 (referred to hereinafter as "the Examiner's Answer"), in an Appeal of the final rejection of claims 1-12, 23 and 25 in the above-identified patent application.

REAL PARTY IN INTEREST

A statement identifying the real party in interest is contained in Appellants' Appeal Brief filed April 27, 2004, and Corrected Appeal Brief, filed July 19, 2004 (referred to herein collectively as "Appeal Briefs").

RELATED APPEALS AND INTERFERENCES

A statement identifying related appeals is contained in Appellants' Supplemental Appeal Brief, filed October 22, 2004 (referred to herein as "Supplemental Appeal Brief")

STATUS OF CLAIMS

A statement identifying the status of the claims is contained in Appellants' Supplemental Appeal Brief.

STATUS OF AMENDMENTS

A statement identifying the status of the amendments is contained in Appellant's Appeal Briefs.

SUMMARY OF INVENTION

A Summary of the Invention is contained in Appellant's Appeal Briefs.

ISSUES PRESENTED FOR REVIEW

A statement identifying the issues presented for review is contained in Appellants' Supplemental Appeal Brief.

GROUPING OF CLAIMS

A statement identifying the grouping of the claims is contained in Appellants' Supplemental Appeal Brief.

CLAIMS APPEALED

A copy of the appealed claims is contained in Appendices of Appellant's Appeal Briefs.

ARGUMENT

Rejections under 35 U.S.C. §112, second paragraph

Claims 4 and 7 are rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

Claim 4

Beginning on page 3, 6<sup>th</sup> paragraph, of the Examiner's Answer, the Examiner stated that, [s]pecific to the limitation of 'without using any knowledge about properties or features of sequences', said limitation causes claim 4, which depends from claim 1, to be vague and indefinite because claim 1 recites 'the sequences are not aligned.' The recitation of 'the sequences are not aligned' in claim 1 has been

reasonably construed as providing ‘knowledge about properties or features of sequences.’

In response to the Examiner’s above remarks, Appellants respectfully re-submit that nothing in the specification indicates that a property or a feature of a sequence that is known or used, e.g., in discovering patterns, includes the fact that the sequences are not aligned, as the Examiner suggests. In fact, claim 4, itself, recites that “discovering is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences.” (emphasis added) Respectfully, one of ordinary skill in the art, given the teachings of claim 4 and the supporting teachings of the specification, would not interpret “without using any knowledge about properties or features of sequences” to include using the fact that the sequences are not aligned, because, if one were to follow this unsubstantiated interpretation, claim 4 would be inconsistent, and make no sense.

For example Appellants, in their previous response pointed out that the specification on page 7, lines 19-23, sets forth the definition of a feature, e.g., in a computational biology context, as,

a combination of amino acids with understood behavior and possibly known 3-dimensional structure. For instance, for a helix-turn-helix (HTH) motif that mediates the binding of many regulatory proteins to regulatory control sites of DNA, the two features are the two helices at the beginning (7 a.a.) and the end (9 a.a.) of the 20 a.a. stretch that corresponds to an instance of the HTH motif.

And the definition of a property as,

an attribute of a feature: in the case of the HTH, a property would be the fact that the two features (helices) are held together through non-polar interactions of their side chains. See *id.* at lines 23-25.

The Examiner in the Examiner’s Answer, page 5, 2<sup>nd</sup> paragraph, however stated that “[a]n exemplary disclosure is not an explicit definition; therefore the exemplary disclosures do not clearly define the argued limitation as asserted by the Appellant.” Appellants respectfully disagree with the Examiner’s assertions. When interpreting the claims, e.g., the meaning of the term “feature” or the term “property,” one should look to the supporting teachings of the specification. Even if by way of example, the teachings of the specification clearly provide one of ordinary skill in the art with guidance on how to interpret these terms. Regardless of whether a “strict definition” of the terms “feature” and “property” according to the Examiner, are provided in the specification, the fact remains that nothing in the present teachings in any way indicates that the sequences not being aligned should be construed as either a feature or a property.

The Examiner, in the Examiner's Answer, page 5, further stated that "Appellants [reference] . . . to page 7, lines 23-25, to argue that said page 'defines property as' [] is not persuasive because the pointed support discloses 'an example of a feature.'" It is unclear from this statement of the Examiner exactly what is being asserted. However, Applicants point out that, as stated above, a  
 5 property may be defined as "an attribute of a feature."

The Examiner, in the Examiner's Answer, page 5, 3<sup>rd</sup> paragraph, stated that,

[s]pecific to the pointed support on page 8, lines 6-7, the disclosure supports that a type of feature of the sequences is derived from aligning the sequences. The same disclosure supports that 'the sequences are not aligned' is also a type of feature  
 10 property. For example, one of ordinary skill in the art would expect two scenarios from discovering similarities (features) between sequences wherein each scenario supports the type of feature described in the instant specification. The first feature results from the sequences being aligned. The second feature results from the sequence being 'not aligned' which represents sequences that are not similar.

15 It is not clear to Appellants exactly what the Examiner means by the above statement. Clarification is respectfully requested. However, Appellants point out that the referenced section of the specification, e.g., page 8, lines 6-7 simply states that previously "researcher knew and exploited properties of sequences, knew and exploited features of the sequences, and/or aligned the sequences."  
 20 This simply indicates that researchers either knew and used properties of the sequences, features of the sequences and/or aligned the sequences, not that a feature or a property is that the sequences are not aligned (as the Examiner suggests).

The Examiner, in the Examiner's Answer, beginning on page 4, 2<sup>nd</sup> paragraph, stated that "the limitation of 'unaligned sequences' causes claim 4 to be vague and indefinite because claim 1, line  
 25 2, from which claim 1 depends, recites 'not aligned.' Claim 4 is unclear whether the limitations are the same." The Examiner further stated in the Examiner's Answer, beginning on page 5, 4<sup>th</sup> paragraph, that,

Appellant argues that the terms 'unaligned' and 'not aligned' are the same. . .  
 . Appellant's argument is not persuasive because the dictionary does not cite 'not  
 30 aligned' as being equivalent to unaligned, but rather 'nonaligned.'

Respectfully, Appellants submit that one of ordinary skill in the art would immediately recognize that the terms "unaligned" and "not aligned" are the same. There simply is no ambiguity in the use of these two terms. It appears to be merely a matter of semantics whether to use "unaligned,"  
 35 "non-aligned" or "not aligned."

Claim 7

In the Examiner's Answer, page 4, 3<sup>rd</sup> paragraph, the Examiner stated that,

Claim 7, lines 1-2, the limitation of 'for one of the positions . . . one expected symbol is a plurality of expected symbols' causes said claim to be vague and indefinite because it is unclear whether 'one of the positions' is occupied by one symbol or a plurality of symbols.

Appellants again respectfully point out that claim 6, from which claim 7 depends, recites, in part, that "each pattern comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol." (emphasis added) Claim 7 recites, in part, that "the at least one expected symbol is a plurality of expected symbols." It is important to keep in mind that this limitation of claim 7 refers to the pattern(s). The specification, at page 13, lines 1-3, for example, indicates that a bracket, e.g., in a pattern, represents a "one of" choice. For instance, the exemplary pattern shown in the specification, at page 25, line 21, illustrates some positions being occupied by "one of" a plurality of symbols. As such, the limitations of claim 7 are not indefinite.

As such, Appellants respectfully request reconsideration and withdrawal of the Section 112 rejections.

Rejections under 35 U.S.C. §101

Claims 1-12, 23 and 25 are rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory algorithm type subject matter. Namely, the Examiner in the Examiner's Answer, page 6, 5<sup>th</sup> paragraph, stated that,

[c]laims 1-12, 23, and 25 are rejected because said claims are directed to a method, system, and an article of manufacture comprising steps for analyzing sequence data without any physical alteration step, which is considered to be non-statutory subject matter. . . [T]he instant invention comprises algorithmic steps for analyzing sequence data without any physical alteration resulted from said analysis.

Appellants respectfully disagree with the Examiner's assertions and again respectfully submit that under Section 101, "any new and useful process, machine, manufacture, or composition of matter" is patentable. 35 U.S.C. §101. It is recognized, however, that despite the broad scope of section 101, "laws of nature, physical phenomena and abstract ideas" cannot be patented. *Diamond v. Chakrabarty*, 447 U.S. 303, 309, 206 U.S.P.Q. (BNA) 193, 197 (1980). The Examiner asserted that claims 1-12, 23 and 25 appear to claim "algorithmic steps for analyzing sequence data." To the contrary, however, each of independent claims 1, 23 and 25 are expressly directed to a practical

application. Namely, in each of claims 1, 23 and 25 it is determined whether a candidate sequence comprises a predetermined number of patterns common to a plurality of unaligned sequences, i.e., to determine whether the candidate sequence is a member of a family. See, for example, page 6, lines 14-15, of the specification. Thus, “the present invention provides a way of determining in an unsupervised manner additional members for a family that is defined initially through exemplar sequences.” Specification, page 6, lines 1-3.

Therefore, each of claims 1, 23 and 25, as well as all claims dependent thereon, are clearly tied to a practical application. A process that is limited to a practical application of an abstract idea or mathematical algorithm in the technological arts is patentable. See Examination Guidelines for Computer-Related Inventions, Section IV. B. 2. b. (ii). In the Examiner’s Answer, the Examiner stated that “Appellant argues ‘each of independent claims 1, 23, and 25 are expressly directed to a practical application . . . Appellant’s argument [is] not persuasive as discussed below.’” See Examiner’s Answer, page 7, 2<sup>nd</sup> paragraph.

However, the Examiner provides no further explanation regarding the claimed invention being tied to a practical application other than to state, for example, that “[s]pecific to the pointed support to assert that the claimed method is directed to a practical application, it is noted that the claimed process . . . does not result in any type of physical alteration.” See, Examiner’s Answer, page 8, 2<sup>nd</sup> paragraph. Thus, no reasoning on the part of the Examiner is provided as to the claimed method being tied to a practical application.

Therefor, for at least the reasons stated above, Appellants submit that each of claims 1-12, 23 and 25 are in full compliance with 35 U.S.C. §101.

#### Rejections under 35 U.S.C. §102

Claims 1-8, 10-12, 23 and 25 are rejected under 35 U.S.C. §102(b) as allegedly unpatentable over Benson. To the extent that the arguments presented in Appellants’ Appeal Brief are pertinent to the present rejections and cited art, those arguments are maintained and incorporated by reference herein. The additional remarks and rejections made by the Examiner in the present Office Action will now be addressed.

#### Claims 1-3

In the Examiner’s Answer, page 9, 2<sup>nd</sup> paragraph, the Examiner stated that,

UniGene comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned), as in instant claim 4. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share [sic.] statistically significant DNA similarity (common patterns) are placed into the same cluster, as in instant claim 5. One important use of the UniGene clusters (set of sequences) is to identify novel and non-redundant sequence candidates that identifies coding sequences in the genome based on predetermined patterns of said clusters, as in instant claims 1-3. (internal citations omitted)

The Examiner makes reference to an NCBI News article, dated August 1996 (hereinafter “NCBI News”) to support the rejections.

Regarding claims 1-3, Appellants respectfully re-submit that clustering sequences, as described in Benson, does not anticipate, nor make obvious, the step of discovering patterns common to a plurality of sequences, e.g., as in claim 1, from which claims 2 and 3 depend. Namely, nowhere does Benson teach or suggest discovering any patterns. Clustering similar sequences simply is not the same as pattern discovery, even if the clustering is based on “significant DNA similarity.” For at least that reason, the teachings of the present claims are neither anticipated nor obvious over Benson.

In the Examiner’s Answer, page 11, 2<sup>nd</sup> paragraph, the Examiner stated that “the limitation of ‘discovering of a plurality of patterns’ has not been explicitly defined in the instant specification.” Appellants respectfully disagree with the Examiner’s assertions. The Specification, for example, beginning on page 2, line 1, describes a descriptor for searching for patterns comprising a series of expected amino acids. A pattern might require certain amino acids to be in one particular location, then allow several locations where any amino acid could reside, and then require only a particular amino acid in a final location. As such, Benson clearly does not teach or suggest discovering patterns.

Thus, for at least the reasons stated above, Appellants respectfully request reconsideration and withdrawal of the rejections of Claims 1-3.

#### Claim 4

Claim 4, as described above, recites that the step of discovering is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences. The Examiner, in the Examiner’s Answer, page 12, 1<sup>st</sup> paragraph, asserted that, by way of reference to Benson and NCBI news, “UniGene comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned).” Respectfully, regardless of whether



Benson/NCBI news teaches incomplete and uncharacterized sequences, this in no way indicates that the sequences are unaligned. In fact, it is unclear to Appellants how the Examiner is arriving at this conclusion.

Appellants respectfully also point out that, without any assertions as to the validity of the Examiner's characterization of the teachings of Benson/NCBI News, the Examiner, in the Examiner's Answer, page 13, 2<sup>nd</sup> paragraph, indicated that according to the teachings of Benson/NCBI News "statistically significant and common patterns are determined by sequence alignments." This statement seems to be in contravention to the earlier statements of the Examiner.

Thus, for at least this reason, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 4.

#### Claim 5

Claim 5 recites, in part, that if the candidate sequence comprises the predetermined number of patterns, then that sequence is added to the set of sequences to create a new set of sequences. The Examiner in the Examiner's Answer stated that, "Benson et al. via NCBI News discloses new EST submissions that do not match any sequences (predetermined threshold) in the UniGene set." Appellants first point out that, as stated above, Benson does not teach or suggest pattern discovery. Therefore, for that reason alone, claim 5 is neither anticipated nor obvious over Benson. Further, Appellants fail to see how an alleged disclosure of sequences which do not match any other sequences can be equated with having a threshold of a predetermined number of patterns that a candidate sequence has to have. The two things are simply not the same.

Thus, for at least this reason, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 5.

#### Claim 8

Claim 8 recites that the step, e.g., of claim 3, of determining if each of the plurality of patterns is statistically significant comprises the steps of selecting one of the patterns, determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold, and continuing to select additional patterns until each pattern has been selected.

For at least the reason, as presented above, that Benson does not teach or suggest pattern discovery, claim 8 is neither anticipated nor obvious over Benson.

The Examiner, in the Examiner's Answer, page 13, stated that, with regard to Benson/NCBI News, "[n]ew EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are organized into unique clusters to provide additional mapping candidates." Appellants respectfully submit that this teaching in Benson/NCI News has absolutely nothing to do with a selected sequence, pattern or other selection meeting a predetermined threshold.

Thus, for at least this reason, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 8.

#### 10 Claim 11

Claim 11 recites that the step, e.g., of claim 3, of determining if each of the plurality of patterns is statistically significant further comprises the steps of if any of the patterns is statistically significant, selecting a statistically significant pattern, modifying a composite descriptor to include the selected pattern if the selected pattern is not already part of the composite descriptor, and continuing to select statistically significant patterns until all statistically significant patterns have been selected.

As above, for at least the reason that Benson does not teach or suggest pattern discovery, claim 11 is neither anticipated nor obvious over Benson. Further, as presented above, NCBI News, in a more detailed explanation of the teachings contained in Benson, merely states that sequences sharing statistically significant DNA sequence similarity in the 3' UTR are assigned to the same cluster. See NCBI News, *Id.* Nothing, therefore, in Benson and/or NCBI News in any way indicates collecting statistically significant information, patterns or otherwise, e.g., in a composite descriptor.

Thus, for at least this reason, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 11.

#### 25 Claim 6

Claim 6 recites, in part, that each pattern, e.g., of claim 1, comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol and other of the plurality of positions comprise positions which may be occupied by any sequence character.

Appellants first resubmit that BLAST, e.g., as described in Altschul et al., entitled, "Basic Local Alignment Search Tool," 215 J. MOL. BIOL. 403-410 (1990) (hereinafter "Altschul") does not involve pattern discovery. For example, BLAST, as referenced in Benson and described in Altschul, does not have anything to do with the processing of sequences in a set of sequences. Namely,

BLAST does not generate anything, pattern or otherwise, from the sequences in a set of sequences. BLAST is in fact a query-driven method that involves processing a query sequence to aid in finding matches with that query in a database of sequences. Specifically, BLAST takes a query sequence and processes it to generate sequential  $k$ -tuples, wherein the value of  $k$  is fixed. For example, see Altschul, page 405, first col., wherein a list of all contiguous  $w$ -mers in the query sequence is generated, e.g., often with  $w = 12$ . The  $k$ -tuples generated are then compared to sequences in a database. See Altschul, *Id.* Therefore, BLAST does not anticipate discovering patterns common to a plurality of sequences in a set of sequences and then determining if a candidate sequence comprises a number of the patterns. For at least this reason, the teachings of the present claims are neither anticipated nor obvious over Benson.

Secondly, BLAST would not be a suitable program to determine whether certain patterns exist in a candidate sequence. As mentioned above, BLAST functions by generating tuples, e.g.,  $w$ -mers, from a query sequence. Trying to match one or more patterns with a sequence, by processing the sequence (as in BLAST) would make finding any matches nearly impossible. Therefore, the teachings of Benson are inconsistent with the present teachings. For at least this reason, the teachings of the present claims are neither anticipated nor obvious over Benson. Thus, for at least that reason, claim 6 is neither anticipated by, nor obvious over, Benson. Further, BLAST does not involve a search criteria having one of either positions that each comprise at least one expected symbol and positions which may be occupied by any sequence character.

In the Examiner's Answer, page 14, 1<sup>st</sup> paragraph, the Examiner states that,

Appellant argues 'BLAST does not involve search criteria having one of either positions that each comprises . . . any sequence character.' It is noted that claims 6 and 7 do not recite the argued 'search criteria limitation.'

Appellants respectfully point out that claim 6 recites that each pattern comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol and other of the plurality of positions comprise positions which may be occupied by any sequence character. Thus, Appellants are unclear as to the above assertions.

Thus, for at least the reasons stated above, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 6.

#### Claim 7

Claim 7 recites, that for one of the positions, e.g., of claim 6, the at least one expected symbol is a plurality of expected symbols. For at least the reason that BLAST does not involve pattern

discovery, as described above in conjunction with the rejection of claim 6, claim 7 is neither anticipated by, or obvious over, Benson. Further, as was highlighted above, e.g., in reference to claim 6, BLAST does not involve a search criteria having positions that each comprise at least one expected symbol, e.g., a plurality of expected symbols.

Thus, for at least this reason, Appellants respectfully request reconsideration and withdrawal of the rejections of claim 7.

Therefore, given the above remarks, Appellants respectfully submit that none of claims 1-8, 10-12, 23 and 25 are either anticipated or obvious over Benson. Thus, Appellants respectfully request reconsideration and withdrawal of the rejections of claims 1-8, 10-12, 23 and 25 under 35 U.S.C. §102(b).

#### Rejections under 35 U.S.C. §103

Claims 1-12 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Benson taken with Kleffe.

First, Appellants respectfully submit that, as presented above, the teachings of the present claims are neither anticipated nor obvious over Benson. Kleffe does not provide any of the limitations for which Benson is lacking. Thus, for at least that reason, claims 1-12 are not obvious over Benson taken with Kleffe.

The Examiner further stated in the Examiner's Answer page 15, 3<sup>rd</sup> paragraph, that "[f]or a given sequence segment, the algorithm of Kleffe et al. produces a set of alternative gene predictions (patterns) that differ in the assignment of splice junctions." Appellants respectfully submit that this teaching in Kleffe does not in any way anticipate patterns. Kleffe discloses, e.g., at page 232, 2<sup>nd</sup> column, that alternative gene predictions are produced that differ in the assignment of splice junctions. There is however, no indication that these gene predictions constitute patterns. Clarification of the Examiner's conclusions is thus respectfully requested.

Given the above remarks, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 1-12 under 35 U.S.C. §103(a).

#### Conclusion

The rejections of the claims under §112, §101, §102 and §103 are believed to be improper and should be withdrawn.

The attention of the Examiner and the Appeal Board to this matter is appreciated.

Respectfully submitted,



Date: July 12, 2005

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